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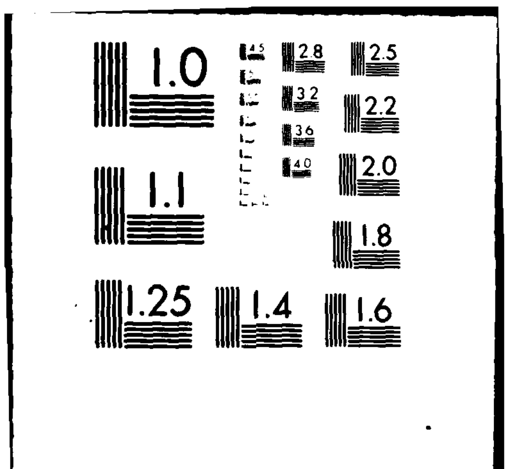
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DEVELOPMENT OF NON-INTRUSIVE AUTOMATED METHODS FOR EVALUATION OF PHYSIOLOGIC FUNCTION IN SEVERELY TRAUMATIZED PATIENTS

FINAL REPORT

by

Sanford J. Larson, M.D., Ph.D.

James J. Ackmann, Ph.D.

Joseph H. Battocletti, Ph.D.

Anthony Sances, Jr., Ph.D.

September, 1979

(For the period 1 May, 1971 through 30 June, 1976)

Supported by

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The objective of this program is to further develop non-invasive patient monitoring techniques, specifically, evoked potentials, EEG, bioelectric impedance, and nuclear magnetic resonance (NMR) flow measurement; to determine the feasibility of applying these techniques in an automated system; and to access the efficacy of the methods for detecting early physiologic changes in severely traumatized patients.

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During the contract period, a computerized monitoring system was developed for automated monitoring of somatosensory evoked potentials , two channels of EEG, bilateral transcranial impedance, transthoracic baseline impedance, tidal volume and respiration rate derived from a transthoracic impedance measurement, intra-arterial blood pressure, intracranial pressure, heart rate and temperature. A total of fifty patients were studied with the system. In addition, two types of NMR blood flowmeters were developed and tested off-line. In the initial phases, only evoked potentials were monitored; the additional variables noted above were added as the program progressed. The technical feasibility of applying the non-evasive methodology for on-line monitoring was demonstrated. Furthermore, the potential for detecting early changes using evoked potential and EEG monitoring was demonstrated. In addition to the on-line studies, off-line studies were conducted in all areas.

The NMR Blood Flowmeter project led to the development and construction of two types of NMR Flowmeters: (1) a cylindrical crossed-coil system operating at 3.2 mHz, applicable to limb blood flow, and (2) a flat single-coil system at 9 mHz, applicable to cerebral blood flow. The cylindrical system was satisfactorily tested on human volunteers; improvements in this system are being undertaken. The flat-coil system was also tests on a human volunteer, but was found to lack the required frequency stability for routine blood flow measurement; a new flat crossed-coil detector is being contemplated.

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SUMMARY

The objective of this program is to further develop non-invasive patient monitoring techniques, specifically, evoked potentials, EEG, bioelectric impedance, and nuclear magnetic resonance (NMR) flow measurement; to determine the feasibility of applying these techniques in an automated system; and to access the efficacy of the methods for detecting early physiologic changes in severely traumatized patients.

During the contract period, a computerized monitoring system was developed for automated monitoring of somatosensory evoked potentials, two channels of EEG, bilateral transcranial impedance, transthoracic baseline impedance, tidal volume and respiration rate derived from a transthoracic impedance measurement, intra-arterial blood pressure, intracranial pressure, heart rate, and temperature. A total of fifty patients were studied with the system. In addition, two types of NMR blood flowmeters were developed and tested off-line. In the initial phases, only evoked potentials were monitored; the additional variables noted above were added as the program progressed. The technical feasibility of applying the non-evasive methodology for on-line monitoring was demonstrated. Furthermore, the potential for detecting early neurologic changes using evoked potential and EEG monitoring was demonstrated. In the present state of development, transcranial impedance measurements appear to be of value in detecting asymmetries and space occupying lesions; however, the confounding effects of scalp edema must be considered. Similarily transthoracic impedance measurements have value for detecting intra-thoracic fluid accumulation and provide an inexpensive and convenient means for monitoring respiration rate and tidal volume. Recent theoretical and experimental evidence developed in our laboratory suggests that measurements of both the real and reactive components of impedance over a wide frequency range coupled with appropriate analysis methods may permit significant improvements in impedance techniques.

In addition to the on-line studies, off-line studies were conducted in all areas. Various electrode systems for obtaining transthoracic baseline impedance and respiratory parameters were investigated.

Various electrode configurations were also investigated for monitoring transcranial impedance. Based on the studies, instruments for on-line monitoring of transthoracic and transcranial impedance were designed and fabricated. In addition to the monitored patients, EEG recordings were obtained in thirteen normal volunteers, seven subjects with Reye's syndrome undergoing exchange transfusions, in seventeen patients with cerebrovascular disorders, and in seventeen normal volunteers matched for sex, age, and basic physical characteristics. Using these data, a peak-detection algorithm was developed for on-line use.

The NMR Blood Flowmeter project led to the development and construction of two types of NMR Flowmeters: (1) a cylindrical crossed-coil system operating at 3.2 mHz, applicable to limb blood flow, and (2) a flat single-coil system at 9 mHz, applicable to cerebral blood flow.

The cylindrical system was satisfactorily tested on human volunteers; improvements in this system are being undertaken. The flat-coil system was also tested on a human volunteer, but was found to lack the required frequency stability for routine blood flow measurement; a new flat crossed-coil detector is being contemplated.

Over the five year duration of the contract, sixteen papers, and twenty-six abstracts were published. In addition, one Master's Thesis and two Doctoral Dissertations were completed.

FOREWARD

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the the Committee on the Guide for Laboratory Animal, Resources, National Academy of Sciences - National Research Council.

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RESULTS: 1 May 1971 through 30 June 1976

I. On-line studies

50 patients, including 40 cases of trauma (20 non-operated, 2 epidural hematoma, 9 subdural hematoma, 3 intracerebral hematoma, 3 gunshot wound, 3 spinal cord injury) and 10 other disorders (4 tumor, 3 aneurysm, 2 AVM, 1 intracerebral hematoma) were studied. Monitoring time varied from 10 hours to 243 hours with a mean of 81 hours. Evoked potentials were monitored in all cases, usually bilateraly. In most patients, recordings were repeated at 1 hour intervals but were sometimes repeated at 30 or 45 minute intervals. The total number of recordings per patient varied from 13 to 243 with a mean of 85.

Conventional parameters and intracranial pressure were selected for monitoring as appropriate to each individual patient. Since impedance methods were under development during much of the study, these variables were not monitored in all patients. Similarily, since EEG methods were under development during much of the study, recordings were obtained on magnetic tape for 10 of the monitored patients, and analyzed retrospectively.

Of the 50 patients studied, 3 had normal polyphasic evoked responses which were stable with times; none of these patients had lateralizing findings, and all recovered. 7 patients had essentially flat responses throughout the monitoring period, an all expired. In the remaining patients, waveshape, amplitude, and symmetry, were variable with time. The variability exceded that experienced in normals. Because of the obvious heterogeneity of the data, strict catagorization of waveforms or correlation of particular types of waveforms with particular neurologic manifestations or outcome was not considered valid. Some generalizations, however, can be made. In the group of 7 patients with essentially flat waveforms all were either flacid or had decerebrate posturing and expired. However in 2 patients, responses were initially flat and then slowly recovered. In patients with angiographic evidence of impaired intracranial blood flow, reduced amplitudes were frequently encountered. In patients with confirmed space-occupying lesions, monophasic responses were generally present.

The EEG recordings demonstrated a clear shift to the lower frequency ranges in the patient population. As with evoked potentials, there were obvious heterogeneities in the data, and time trends in individual patients varied considerably. In 8 of the 10 patients, frequency asymmetries were observed. The asymmetries correlated with clinical manifestations and with evoked potential data. In general, a lower percentage of delta activity and a higher mean frequency correlated with increased responsiveness

The most significant finding of the on-line studies is that evoked potential and EEG parameters show changes in advance of detectable clinical changes. While it can not be concluded on the basis of this study that changes always precede clinically observable neurologic changes, the findings suggest that this occurs sufficiently often to justify further investigation.

II. Off-line studies

A. EEG

In the early phases of the study, period measurements between zero crossings were used to classify halfwaves into the cannonical EEG frequency bands. The algorithm was suitable for recordings obtained from normals and was also used successfully in a study of stroke patients. However, baseline drift secondary to patient movement made the algorithm unsuitalbe for on-line use in trauma patients. Recordings were therefore obtained in 10 of the monitored patients, from 16 normal volunteers in the awake state, from 3 sleep subjects, and from 7 coma patients with Reye's syndrome. Using these recordings, an algorithm was developed for peak-trough detection. Artifact discriminators for excessive amplitude and low frequency were included. The algorithm computes the percentage time spent in the cannonical frequency bands, the average amplitude and frequency within the bands, the percentage artifact, the mean overall frequency, and the mean overall peak-trough amplitude for continous 1 minute analysis epochs. Using the above described data, an analysis of variance was carried out to determine which parameters are most suitable for trend monitoring in comatose subjects. Based on these analyses, the percentage delta activity and mean frequency were selected. Following parameter determination, a tracking procedure was implemented for detection of statistically significant changes.

B. Impedance Studies

1. Transcranial

Studies were directed toward measurements of current density and intracerebral impedance in animals and transcranial baseline impedance in both animals and humans. Early studies demonstrated the frequency dependance of both intracerebral and surface impedance measurements. In monkeys, intracerebral increases secondary to hypoxia were approximately 3 times as great at 1 kHz as compared to changes at 10 kHz. At lower frequencies, the measurements more closely reflect changes in the extracellular space since less current penetrates the cell membrane through the capacitive element. Based on these experiments, an initial study was conducted in human volunteers and head injury patients. In normals, an average impedance of 87Ω with a range of 55-112 and a standard deviation

of 11Ω was observed. In contrast, impedance in patients with head injury and space occupying lesions varied from 25 to 65Ω with an average value of 40Ω. While measurements in the first 10 patients in the on-line study suggested potential for detecting intracranial mass effects, on-line monitoring was complicated by the confounding effects of scalp edema. Therefore, both theoretical and analog studies of different electrode configurations were undertaken. It was determined that injecting current from glabella to inion and deriving potential measurements form the outermost EEG/evoked potentials electrodes rendered the measurements less sensitive to scalp edema and somewhat more sensitive to intracranial lesions. The system has the advantage that only two additional electrodes must be added to the normal montage, and that asymmetries can be detected readily.

In an off-line pilot study of 15 normal volunteers, the average impedance was 15.3Ω with a standard deviation of 1.3Ω and a range of 12-17Ω. The percent variation between hemispheres ranged from zero to 4.2% with a mean of 1.9% and a standard deviation of 1.4%. In 10 patients with space-occupying lesions demonstrated by CT scans and confirmed at surgery, average impedance on the unaffected side was 16.5Ω with a range of 13.4 to 22; average impedance on the side of the lesion was 12.5Ω with a range of 11.0 to 15.0. Asymmetries ranged from 20.0 to 46.7% with a mean difference of 40.0%. Thus, while baseline values overlap, there are statistically significant differences in symmetry with unilateral space-occupying lesions.

2. Transthoracic

In order to obtain reasonable signal-to-noise ratios, measuring currents in the millamp range were used in many previous studies. For safety reasons, frequencies above 20 kHz were used since thresholds of vagal stimulation and ventricular fibrillation increase with frequency. Instrumentation developments in recent years have made it possible to use measuring currents of less than 25μA. This level is well below the threshold of sensation thus permitting safe measurements at low frequencies. An instrument was therefore designed using a $2kH_z$, 25μA constant current source. Provisions were included for both baseline impedance and tidal volume.

Theoretical considerations suggest that measurements at lower frequencies should have a greater sensitivity to extracellular edema. This was partially confirmed in a volume overload study in dogs.

Tidal volume calibration studies were conducted in 7 normal volunteers. The instrument is linear within 5% over a range of tidal volumes from 0.3 to 2 liters but requires

calibration for each individual subject. The instrument was used on-line in the last 5 patients in the study. In 4 of the patients, pulmonary status was normal and transthoracic baseline impedance was stable at approximately 25Ω. In the 5th patient, there was radiographic evidence of pulmonary edema. Baseline impedance increased from 18Ω to 26Ω as the edema resolved over a two-day period.

C. NMR

NMR blood flow research between May 1, 1971 and June 30, 1976 developed at a steady pace from the simple application of NMR techniques, to the development of a Limb Flowmeter, and the beginning of research on cerebral blood flow measurement. References listed at the end of this final report, demonstrate this steady progress. The Medical College of Wisconsin has been at the forefront of NMR blood flowmeter research during this period of time.

It became clear to us in early 1973, that a two-magnet system was not practicable, due to the short value of relaxation time, T_1, in a low magnetic field. (Ref. 1, 2) Therefore, emphasis has been placed almost exclusively on single-magnet systems. (Ref. 3-9)

The NMR Blood Flowmeter project led to the development and construction of 2 types of NMR flowmeters: (1) a 12.5 cm I.D. cylindrical crossed-coil system, operating at 3.2 MHz, has been fabricated for blood flow measurement in limbs; (2) a flat single-coil detector, operating at 9 MHz, has been fabricated for cerebral blood flow measurement.

1. Cylindrical NMR Limb Flowmeter

A brief description of the 12.5 cm I.D. cylindrical NMR Limb Flowmeter is given in Appendix A, which is Reference 5. The lumen is large enough to accept the upper limbs of adult humans, and lower limbs of children.

In preliminary studies, arterial blood flow in the forearms of 15 adult human volunteers was measured. Signal amplitudes varied from person to person, as expected, but no quantification was attempted. The effects of hyperemia due to complete occlusions and hand exercise were observed.

Arterial blood flow was measured in both the intact hind limb of a dog, and in its isolated femoral artery. (Ref. 6) By this test, it was demonstrated that the signals obtained in-vivo are produced by blood flow and not be mechanical changes of the arterial wall. System modifications to improve and extend the application of the NMR Limb Flowmeter were undertaken as a result of these preliminary studies.

2. Single-coil Flowmeter

The single-coil NMR flowmeter which has been developed uses a large 2000 Gauss water-cooled electromagent (Walker Scientific Co.) and a super regenerative NMR detector. The main results obtained with the flowmeter are summarized in Appendix B, which is Reference 8. In addition to in-vitro tests, carotid blood flow and jugular vein blood flow were measured. The single-coil/super-regenerative type NMR detector has been unsatisfactory because of a frequency instability due to the fact that the detector coil itself is used as the tuning element of the detector oscillator. A new type of flat crossed-coil detector is being considered which would circumvent this difficulty and posess the advantages of the cylindrical crossed-coil detector.

3. Theoretical Models

Analysis of theoretical models of NMR blood flowmeters have been made throughout the development and testing periods: (1) to aid in their design, and (2) to lead to a better understanding of the physical phenomena occurring in their operation, so that improvements could be made.

LITERATURE CITED

1. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Halbach, R.E., Evans, S.M., Bowman, R.L., Kudravcev, V. and Genthe, W.K.: Nuclear magnetic resonance T_1 relaxation times of blood. Proc 26th Ann Conf on Engin in Med and Biol, 302, 1973.

2. Brooks, R.A., Battocletti, J.H., Sances, A., Jr., Larson, S.J., Bowman, R.L. and Kudravcev, V.: Nuclear magnetic relaxation in blood. IEEE Trans Biomed Engin 22:12-18, 1975.

3. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Evans, S.M., Bowman, R.L., Kudravcev, V. and Ackmann, J.J.: Clinical applications and theoretical analysis of NMR blood flowmeters. Biomed Engin (London) 10(1):12-15, 1975.

4. Sances, A., Jr., Ackmann, J.J., Larson, S.J., Cusick, J.F., Hemmy, D.C., Holst, R.A., Worman, L., Battocletti, J.H., Bernhard, V., Barr, R., Cohen, B., Cunha, S.X. and Bravo-Fernandez, E.: Non-intrusive evaluation of trauma patients. Proc Int'l Federation of Automatic Control, 6th Triennial World Congress, Boston, Mass., 47.3, 1975.

5. Halbach, R.E., Battocletti, J.H., Sances, A., Jr., Larson, S.J., Evans, S.M., Bowman, R.L. and Kudravcev, V.: A single sideband NMR arm flowmeter. Proc 28th Ann Conf Eng Med Biol 17:112, 1975.

6. Sances, A., Jr., Malfertheiner, P., Battocletti, J.H., Larson, S.J., Halbach, R.E., Evans, S.M., Bowman, R.L., Fegiz, G. and Ray, L.: Techniques for non-invasive nuclear magnetic resonance blood flow measurement. Surgery in Italy 9(3):186-194, 1976.

7. Sances, A.,Jr., Battocletti, J.H., Halbach, R.E., Larson, S.J., Evans, S.M., Bowman, R.L. and Kudravcev, V.: Limb blood flow measurement by nuclear magnetic resonance. Digests of 11th Int'l Conf Med Biol Engin, Ottawa, Canada, 430-431, 1976.

8. Battocletti, J.H., Sances, A., Jr., Bowman, R.L., Kudravcev, V., Halbach, R.E., Larson, S.J., Evans, S.M. and Cusick, J.F.: Cerebral blood flow measurement using nuclear magnetic resonance techniques. Proc. 29th Ann Conf Eng Med Biol, Boston, Mass., 17:42, 1976.

9. Halbach, R.E., Battocletti, J.H., Sances, A., Jr. and Evans, S.M.: Limb blood flow monitoring by an NMR probe. Clinical Research 24:559A, 1976.

PUBLICATIONS (Supported wholly or in part by Contract No. DADA17-71-C-1093)

1. Bowman, R.L., Kudravcev, V., Battocletti, J.H., Larson, S.J., and Sances, A., Jr.: A non-invasive nuclear magnetic resonance flowmeter. Proc Workshops 9th Int'l Conf Med and Biol Eng, Melbourne, Australia, No. 2:6-12, 1971.

2. Jarzembski, W., Sances, A., Jr., Larson, S.J. and Cunha, S.: A method for observing transcranial changes in the head injury patient. Proc 7th Ann Mtg AAMI, April 24-26, 1972, Las Vegas, Nevada. (Presented)

3. Jarzembski, W.B., Larson, S.J. and Sances, A., Jr.: Cerebral current density measurements during application of electrical currents through surface electrodes. Chapter in Physiological Applications of Impedance Plethysmography, R.D. Allison, ed., ISA, Pittsburgh, Penn., 1972, pp. 31-42.

4. Lessard, C.S.: Electroencephalographic signal evaluation during sleep and in coma. Doctoral Dissertation, Marquette University, Milwaukee, Wisconsin, May 1972.

5. Battocletti, J.H., Linehan, J.H., Hosek, R.S., Sances, A., Jr., Halbach, R.E., Itskovitz, H.D., Larson, S.J., Evans, S.J., Bowman, R.L. and Kudravcev, V.: NMR blood flow measurement in an isolated perfused kidney. Submitted to Proc 25th Ann Conf Eng and Med Biol, 146, 1972.

6. Battocletti, J.H., Linehan, J.H., Larson, S.J., Sances, A., Jr., Bowman, R.L., Kudravcev, V., Genthe, W.K., Halbach, R.E. and Evans, S.J.: Analysis of a nuclear magnetic resonance blood flowmeter for pulsatile flow, IEEE Trans Biomed Engin 19:403-7, 1972.

7. Ackmann, J.J., Larson, S.J., Sances, A., Jr., Reigel, D.H., Battocletti, J.H., Jarzembski, W.B., Dallmann, D.E., Bowman, R.L. and Kudravcev, V.: Computerized non-invasive monitoring of the trauma patient. Proc 25th Ann Conf Eng and Med Biol, 106, 1972.

8. Wang, Oliver Shyi-Lin: Tracer measurements of periodic flow in a tube using a NMR flowmeter and its physiologic application. Master's Thesis, Marquette University, Milwaukee, Wisconsin, December 1972.

9. Larson, S.J., Sances, A., Jr., Ackmann, J.J. and Reigel, D.H.: Non-invasive evaluation of head trauma patients. Surgery 74:34-40, 1973.

10. Lessard, C.S., Sances, A., Jr. and Larson, S.J.: Period analysis of EEG signals during sleep and post-traumatic coma. Proc 44th Annual Meeting of Aerospace Medical Association, Las Vegas, Nevada, May 7-10, 1973.

11. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Halbach, R.E., Bowman, R.L., Kudravcev, V. and Evans, S.M.: NMR detection of low magnetization levels in flowing fluids. IEEE Trans Mag 9(3):451-4, 1973.

12. Hosek, R.S., Sances, A., Jr. and Larson, S.J.: On the relationship between scalp-recorded potentials and underlying cortical activity. Proc 26th Ann Conf on Eng in Med and Biology, 105, 1973.

13. Osborne, D., Bernhard, V.M. and Jarzembski, W.B.: Application of impedance rheography to the peripheral vascular system. Proc 26th Ann Conf on Engin in Med and Biol 68, 1973.

14. Jarzembski, W.B.: Forced impedance and guarding for physiological impedance measurements. Proc 26th Ann Conf on Engin in Med and Biol 15:65, 1973.

15. Cohen, B.A., Bravo-Fernandez, E.J. and Hosek, R.S.: Analysis of serial EEGs in patients with cerebrovascular disorders. Proc 26th Ann Conf on Engin in Med and Biol, 397, 1973.

16. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Halbach, R.E., Evans, S.M., Bowman, R.L., Kudravcev, V. and Genthe, W.K.: Nuclear magnetic resonance T_1 relaxation times of blood. Proc 26th Ann Conf on Engin in Med and Biol, 302, 1973.

17. Linehan, J.H., Battocletti, J.H., Wang, O.S., Sances, A., Jr., Larson, S.J., Bowman, S.M., Kudravcev, V. and Evans, S.M.: In vitro study of the NMR flowmeter for pulsatile flow in straight, tapered and bifurcated tubes. Proc 26th Ann Conf on Engin in Med and Biol, 301, 1973.

18. Messavage, L. and Jarzembski, W.B.: Brain impedance as a function of pO_2 and pCO_2. Proc 26th Ann Conf on Eng in Med and Biol, 66, 1973.

19. Larson, S.J., Sances, A., Jr., Reigel, D.H., Meyer, G.A., Dallmann, D.E. and Swiontek, T.: Neurophysiological effects of dorsal column stimulation in man and monkey. J Neurosurg 41(2):217-223, August 1974.

20. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Evans, S.M., Bowman, R.L., Kudravcev, V. and Halbach, R.E.: A review of nuclear magnetic resonance techniques applied to biological systems. Chapter in Biologic and Clinical Effects of Low-Frequency Magnetic and Electric Fields, Llaurado, Sances and Battocletti, eds., C.C. Thomas Publ. Co., Springfield, Illinois, 1974, pp. 263-294.

21. Llaurado, J.G., Sances, A., Jr. and Battocletti, J.H., (eds.): Biologic and clinical effects of low-frequency magnetic and electric fields, C.C. Thomas Publ. Co., Springfield, Illinois, 1974, 345 pages.

22. Battocletti, J.H., Evans, S.M., Larson, S.J., Antonich, F., Bowman, R.L., Kudravcev, V., Sances, A., Jr., Linehan, J.H., Halbach, R.E. and Genthe, W.R.: Measurement of blood flow by nuclear magnetic resonance techniques. Chapter in Flow, Its Measurement and Control in Science and Industry Vol. 1, Part 3 Flow Measurement and Control, Biologic Fluid Flows, W.E. Vannah and H. Wayland, eds., Instrument Society of America, Pittsburgh, Pennsylvania, 1974, pp. 1401-1409.

23. Cohen, B.A., Bravo-Fernandez, E.J., Sances, A., Jr., Makowski, G.G. and Saltzberg, B.: Computer analysis of electroencephalograms on stroke patients. Proc 27th Ann Conf Eng Med Biol, 144, 1974.

24. Houge, J., Sances, A., Jr. and Macur, R.: A microminiature iridium oxide pH electrode and its in vitro evaluation. Proc 27th Ann Conf Eng Med Biol, 400, 1974.

25. Swiontek, T.J., Sances, A., Jr., Larson, S.J. and Jarzembski, W.B.: Comparison of the electrical current distribution from three spinal electrode systems. Proc 27th Ann Conf Eng Med Biol, 248, 1974.

26. Barr, R.E., Ackmann, J.J., Harrington, G.J., Sances, A., Jr. and Saltzberg, B.: Parametric tracking of the EEG in coma using a peak-detection technique. Proc 27th Ann Conf Eng Med Biol, 147, 1974.

27. Harrington, G.J., Ackmann, J.J., Varma, R.R. and Barr, R.E.: Electroencephalographic monitoring of exchange transfusions in Reye's syndrome. Abstracts of the Child Neurology Society Meeting, Madison, Wisconsin, October 1974, p. 25.

28. Battocletti, J.H., Linehan, J.H., Wang, O.S., Sances, A., Jr., Larson, S.J., Evans, S.M., Itskovitz, H.D., Bowman, R.L. and Kudravcev, V.: Organ blood flow measurement using NMR. Digests Intermag Conf, Toronto, Canada, Paper No. 35-8, 1974.

29. Ackmann, J.J., Holst, R.A., Sances, A., Jr. and Larson, S.J.: Transthoracic bioelectric impedance in induced pulmonary edema. Proc 7th Ann Mtg Neuroelectric Society, New Orleans, La., Nov. 1974, pp. 38-39.

30. Brooks, R.A., Battocletti, J.H., Sances, A., Jr., Larson, S.J., Bowman, R.L. and Kudravcev, V.: Nuclear magnetic relaxation in blood. IEEE Trans Biomed Engin 22:12-18, 1975.

31. Battocletti, J.H., Sances, A., Jr., Larson, S.J., Evans, S.M., Bowman, R.L., Kudravcev, V. and Ackmann, J.J.: Clinical applications and theoretical analysis of NMR blood flowmeters. Biomed Engin (London) 10(1):12-15, 1975.

32. Sances, A., Jr., Ackmann, J.J., Larson, S.J., Cusick, J.F., Hemmy, D.C., Holst, R.A., Worman, L., Battocletti, J.H., Bernhard, V., Barr, R., Cohen, B., Cunha, S.X. and Bravo-Fernandez, E.: Non-intrusive evaluation of trauma patients. Proc Int'l Federation of Automatic Control, 6th Triennial World Congress, Boston, Mass., 47.3, 1975.

33. Halbach, R.E., Battocletti, J.H., Sances, A., Jr., Larson, S.J., Evans, S.M., Bowman, R.L. and Kudravcev, V.: A single sideband NMR arm flowmeter. Proc 28th Ann Conf Eng Med Biol 17:112, 1975.

34. Ackmann, J.J., Barr, R.E., Larson, S.J., Sances, A., Jr., Hemmy, D.C. and Cusick, J.F.: Automated monitoring of evoked potentials and EEG in head injury. Proc 28th Ann Conf Eng Med Biol 17:519, 1975.

35. Barr, R.E.: Parametric tracking of the electroencephagram in coma using a computerized peak-detection method. Ph.D. Dissertation, Marquette, University, Milwaukee, Wisconsin, August 1975.

36. Sances, A., Jr., Malfertheiner, P., Battocletti, J.H., Larson, S.J., Halbach, R.E., Evans, S.M., Bowman, R.L., Fegiz, G. and Ray, L.: Techniques for non-invasive nuclear magnetic resonance blood flow measurement. Surgery in Italy 9(3):186-194, 1976.

37. Sances, A., Jr., Battocletti, J.H., Halbach, R.E., Larson, S.J., Evans, S.M., Bowman, R.L. and Kudravcev, V.: Limb blood flow measurement by nuclear magnetic resonance. Digests of 11th Int'l Conf Med Biol Engin, Ottawa, Canada, 430-431, 1976.

38. Battocletti, J.H., Sances, A., Jr., Bowman, R.L., Kudravcev, V., Halbach, R.E., Larson, S.J., Evans, S.M. and Cusick, J.F.: Cerebral blood flow measurement using nuclear magnetic resonance techniques. Proc 29th Ann Conf Eng Med Biol, Boston, Mass., 18:42, 1976.

39. Halbach, R.E., Battocletti, J.H., Sances, A., Jr. and Evans, S.M.: Limb blood flow monitoring by an NMR probe. Clinical Research 24:559A, 1976.

40. Ackmann, J.J., Seitz, M.A., Dawson, C. and Sances, A., Jr.: Complex bioelectric impedance measurements for the detection of pulmonary edema. Digest of the 11th Int'l Conf Med and Biol Engin, Ottawa, Canada, 1976, pp. 288-289.

41. Barr, R.E. and Ackmann, J.J.: A method for computerized statistical monitoring of the EEG. Proc 29th Ann Conf Eng Med Biol 18:218, 1976.

42. Ackmann, J.J., Sances, A., Jr. and Larson, S.J.: Tutorial: Non-invasive monitoring of the head injury patient. Proc 29th Ann Conf Eng Med Biol 18:465, 1976.

43. Barr, R.E. and Ackmann, J.J.: Computerized statistical monitoring of the EEG in intensive care management. Proc IEEE Region V Ann Conf, April 1976, pp. 219-222.

44. Ackmann, J.J., Sances, A., Jr., Larson, S.J., Seitz, M.A. and Dawson, C.A.: Applications of bioelectric impedance in trauma. Digest of the 2nd Int'l Conf Bioelectric Impedance, Lyon, France, June 16-19, 1976, pp. 119-124.

45. Barr, R.E., Ackmann, J.J., Harrington, G.J., Varma, R.R., Lewis, J.D. and Caspar, J.T.: Computerized evaluation of electroencephalographic changes accompanying exchange transfusion in Reye's syndrome. Electroenceph Clin Neurophysiol 42:466-479, 1977.

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A SINGLE SIDE-BAND NUCLEAR MAGNETIC RESONANCE ARM FLOWMETER

Halbach, R., Dept. of Neurosurgery, Medical College of Wisconsin
Battocletti, J., Dept. of Neurosurgery, Medical College of Wisconsin
Sances, A., Jr., Dept. of Neurosurgery, Medical College of Wisconsin
Larson, S.J. Dept. of Neurosurgery, Medical College of Wisconsin
Evans, S.M., Dept. of Neurosurgery, Medical College of Wisconsin
Bowman, R. National Heart and Lung Institute
Kudravcev, V. National Heart and Lung Institute

Nuclear magnetic resonance (NMR) holds promise as a tool for the non-invasive measurement of arterial or venous blood flow in limbs. The hydrogen nuclei, available in abundance in blood, possess a magnetic dipole and a rotational spin moment and can therefore be made to precess under the influence of applied fields.

Following the application of a magnetic field, B_D, to a randomly oriented sample, a small but significantly greater number of magnetic dipoles will align themselves parallel with, rather than against, the field. This population difference or net magnetization rises to equilibrium, M_o, exponentially as follows

$$M = M_o\,(1 - e^{-t/T_1})$$

where T_1 is the longitudinal relaxation time (0.4 - 0.6 s. for blood) and $M_o \cong 0.8$ microgauss at B_D = 748 gauss. The precession frequency of the nuclei is directly proportional to B_D and the gyromagnetic ratio γ or $\omega_o = B_D\,\gamma$; $\omega_o/2\pi$ = 3.192 MHz for B_D = 748 gauss.

To avoid the receiver sensitivity limitations of previously designed single frequency systems, a single side-band limb flow meter was designed with the transmitter at 3.192 MHz and receiver at 3.200 MHz separated in frequency by a modulation field at 8 kHz. A 748 gauss B_D field is supplied by ceramic magnets mounted inside a steel box and trimmed and field stabilized by current in a pair of coils surrounding the poles (Figure 1).

The receiver has a 1 kHz band width 3.2 MHz crystal input filter and very low noise dual gate FET followed by a similar filter and heterodyne conversion to a 2600 Hz IF, which further limits band width to 50 Hz. An operational amplifier, precision rectifier, and low pass filter complete the signal conditioning. The sensitivity of the receiver for unity signal to noise ratio is approximately 100 nanovolts.

The detector structure consists of two pairs of saddle coils for the transmitter and modulator, and a solenoidal receiver coil, all mounted around a 12.5 cm I.D. fiberglass tube in which the arm is placed (Figure 2). An upstream "tagger" coil, when energized at a frequency corresponding to the local field resonance frequency, will reduce the net magnetization of blood passing within it to zero.

In the tag-detect mode the tag coil is periodically energized to randomize a bolus of fluid. Passage of this bolus some time, T, later into the receiver will result in a reduction of the side-band signal generated. The velocity of flow can then be determined as a function of T and coil spacing.

In vitro tag-detect studies with blood flowing through a 3.2 mm I.D. tube have yielded detectable signals at flow rates as low as 25 ml/min, levels that correspond to those expected in vivo. Tag-detect signals have also been recorded down to 20 ml/min with water passing via a 3.2 mm I.D. tube through a saline filled cylinder simulating the arm.

B_D FIELD STRUCTURE

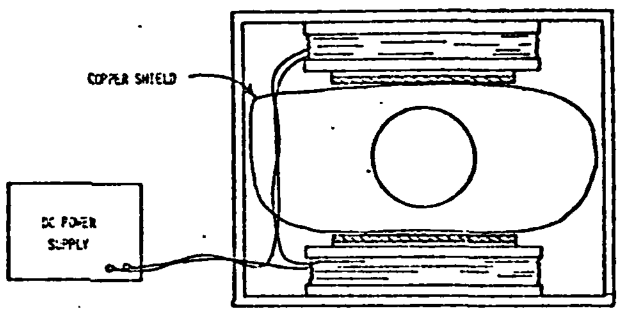

Figure 1.

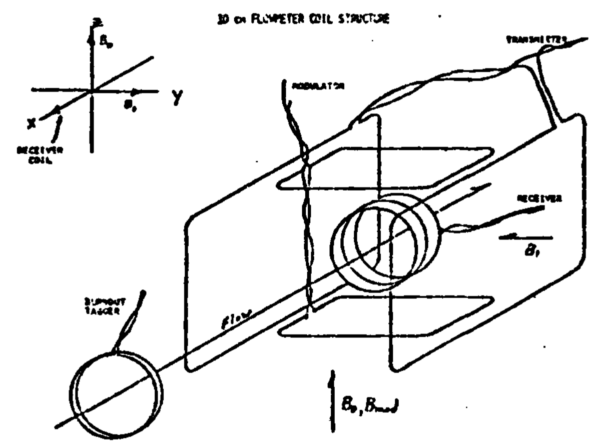

Figure 2.

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Mailing address:
Richard Halbach
Department of Neurosurgery
The Medical College of Wisconsin
8700 West Wisconsin Avenue
Milwaukee, Wisconsin 53226

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CEREBRAL BLOOD FLOW MEASUREMENT USING NUCLEAR MAGNETIC RESONANCE TECHNIQUES

Battocletti, J.H., Sances, A., Jr., Bowman, R.,* Kudravcev, V.,*
Halbach, R.E., Larson, S.J., Evans, S.M. and Cusick, J.F.
Department of Neurosurgery, The Medical College of Wisconsin
*Technical Development Laboratory, National Heart and Lung Institute

Human common carotid arterial and internal jugular vein blood flows have been detected with a single pancake coil super-regenerative nuclear magnetic resonance (NMR) detector, operating at 8.3 MHz. The magnetic field flux density was approximately 1940 gauss.

The NMR blood flowmeter is dependent upon magnetic moments in the nucleus of the hydrogen atom. Since blood is approximately 83% water, there is an abundant number of hydrogen atoms; the nuclear magnetic susceptibility of blood is 3.229×10^{-9} (1). The nuclear magnetic moments can be aligned and rotated by externally applied D-C and A-C magnetic fields. In the NMR flowmeter, blood is magnetized (that is, nuclear magnetic moments are aligned) at one area, and the magnetization is detected at a second downstream region.

For the venous studies, the head is placed in the 1940 gauss field. The magnetized blood at the confluence of the sinuses is demagnetized briefly with a coil energized by a strong radio-frequency current. This tagged portion of the blood is detected at the internal jugular vein. The amplitude of the detected NMR signal is proportional to the volume flow rate (2), while the time delay between the tagging signal and the detected NMR signal is inversely proportional to the flow velocity. This method can be used to evaluate regional differences in cerebral blood flow.

For the arterial studies, the upper thorax and neck are placed in the 1940 gauss field. The pulsatile magnetized blood can be detected over the common carotid artery (1). It can be shown that the peak-to-peak amplitude of the detected NMR signal is porportional to flow rate (2).

Figure 1 demonstrates an in vitro simulation of the venous test, using flowing water in a 6.4 mm I.D. tube. Time delay between the tagging signal and the detected NMR signal increases as flow rate decreases. Figure 2 shows venous signals from an adult human. The time delay between the peaks of the tag and the response is approximately two seconds. Time per division for both Figure 1 and Figure 2 is 0.64 s.

The NMR output signal from the common carotid artery of an adult human is compared with the output of a photoelectric finger plethysmograph. Time per division is 0.256 s.

Fig. 1. In vitro venous test; diagonal lines join peaks of NMR signals.

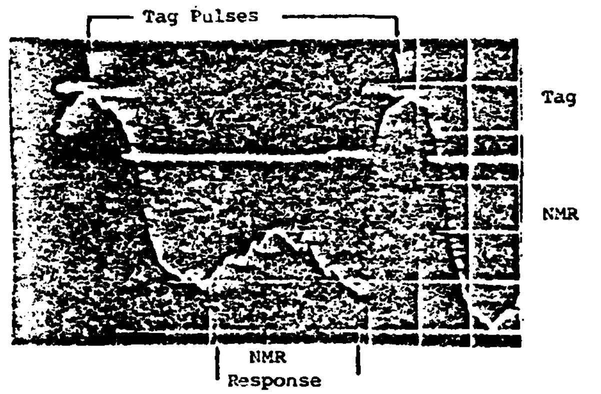

Fig. 2. In vivo venous test.

Fig. 3. In vivo common carotid arterial test.

References:
1) Battocletti, J.H., Sances, A., Jr., Larson, S.J. Evans, S.M., Bowman, R.L, Kudravcev, V., and Halbach, R.E.: A review of nuclear magnetic resonance techniques applied to biological systems. In Biologic and Clinical Effects of Low-Frequency Magnetic and Electric Fields, C.C.Thomas, Springfield, Ill., 1974, Ch. XXII, pp. 263-294.
2) Battocletti, J.H., Sances, A., Jr., Larson, S.J. Evans, S.M., Bowman, R.L., Kudravcev, V., Ackmann, J.J.: Clinical applications and theoretical analysis of NMR blood flowmeters. Biomedical Engineering (London) 10(1):12-15, 20, Jan., 1975.

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Mailing address:
Department of Neurosurgery
8700 West Wisconsin Avenue
Milwaukee, Wisconsin

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